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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,573	04/06/1999	DAVID R. WALT	A-67207-2/DJB/RMS/DCF	6459

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/287,573	WALT ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2005 and 27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-27 and 29-48* is/are pending in the application.

4a) Of the above claim(s) *16-19,23-26,40-45 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-22, 27, 29-39, 46, and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *16-27 and 29-48* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 20, 2005 has been entered.

Amendment Entry

2. Applicant's amendment and response filed December 20, 2005 and April 27, 2006 are acknowledged and entered. Claims 27 and 32-39 have been amended. Claims 16-19, 23-26, 40-45, and 48 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Currently, claims 16-27 and 29-48 are pending. Claims 20-22, 27, 29-39, 46, and 47 are under examination.

Rejections Withdrawn

3. All rejections not reiterated herein have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 20-22, 27, 29-39, 46, and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 is vague and indefinite because it is unclear how the at least first target analyte interrelates to the first bioactive agent and the second bioactive agent in order to thus produce a signal, especially in light of an undefined method recited in the preamble. It appears that a binding interaction between the at least first target analyte and any one of the first and/or the second bioactive agent should take place in order to obtain a measurable response signal from the first and second subpopulations of sensor elements. Please clarify.

Claim 27 is ambiguous in reciting, "first target analyte" because there does not appear to be a "second target analyte" recited in the given set of claims. If there is no second target analyte, it is unclear why the target analyte is referred to as a "first" target analyte.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 20-22, 27, 29-39, 46, and 47 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 39-48 of issued application number 08/944,850 in view of Bierre et al. (US Patent 5,739,000). Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions recite fiber optic bundle assay methods of measuring binding between analyte and subpopulations of sensor elements having different binding partners present in a sensor array and wherein statistical validity of the assay is determined based on the statistical analysis results obtained from each individual measurements of response signals in the array.

ASN 08/944,850 differs from the instant invention in failing to teach specific statistical analysis encompassing exclusion of outlying beads from subpopulations, calculation of mean and standard deviation between measurements, evaluation of statistical validity on the measurements, evaluation using confidence intervals, performance of hypothesis testing and cluster analysis, and comparative evaluation between statistical analyses, as recited in claims 31-39.

Bierre et al. disclose a method of multiparameter data analysis which employs analyzing data obtained from population hierarchy measurements, wherein different cell populations are not mutually exclusive. Bierre et al. specifically obtained measurements to collect a plurality of parameters for each particle (bead) in a sample and performed statistical analysis on the obtained measurements. Statistical analyses performed include calculating a mean and standard deviation, evaluating statistical validity by defining and selecting particles into mutually exclusive clusters and subclusters, i.e. cluster analysis, and repeating statistical analysis for purposes of comparing and evaluating confidence intervals between measurements. See claims 1-3, 6, 11, and 12.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Bierre into the method of ASN 08/944,850 using optical fiber array having a plurality of subpopulations to individually measure the presence of target analytes in the fiber optic bundle because Bierre specifically taught that statistical analysis of cell or particle populations such as those in an array as in the method of ASN 08/944,850, presents a user with great flexibility in defining distinct and overlapping populations of particles or beads for use in subsequent examination. Additionally, statistical analysis, i.e. calculating mean/average, standard deviation, precision/ repeatability of a method as reflected in a second analysis, confidence intervals, correlation studies, and distribution/cluster analysis is standard laboratory practice used to establish optimal values in optimization procedures.

6. Claims 20-22, 27, 29-39, 46, and 47 are rejected under 35 U.S.C. 103(a) as being obvious over Walt et al. (issued ASN 08/944,850) in view of Bierre et al. (US Patent 5,739,000).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

See discussion of ASN 08/944,850 - Walt et al. and Bierre et al. supra.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is noted that in claim 27, step b), a response signal at said sensor elements of at least one of the subpopulations is produced; step c), individual response signals at each of the sensor elements from at least one of the subpopulations are obtained; and step d) a statistical analysis on the response signals from at least one of the subpopulations are performed. Accordingly,

7. Claims 27, 29-39, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al. (US Patent 5,837,196) in view of Bierre et al. (US Patent 5,739,000).

Pinkel et al. disclose a method of simultaneous individual measurements of target analytes in an optical fiber array having a plurality of subpopulations of identical sensor elements (optical fibers bundled together bearing a single type species). Pinkel et al. specifically teach contacting the optical fiber array with a sample comprising target analytes and then detecting production of response signals. Each sensor element is uniquely addressed and each subpopulation bears distinct bioactive agents (biological binding partner); the optical fiber array bears multiple species of bioactive agents (see column 3, line 39 to column 4, line 26 and column 14, lines 36-43). The bioactive agents include nucleic acids, oligonucleotides, and proteins (see column 3, lines 8-22, column 4, lines 27-34 and 55-67 and column 6, lines 30-39). Pinkel et al. provide that use of concave or convex sensor ends results to a greater surface area upon which to

immobilize the bioactive agents to thus, increase the signal to noise ratio per optical fiber of the biosensor (see column 8, lines 22-25). The substrate is either glass or plastic (see column 11, lines 50-55). The detector can be arranged to read individual response signals simultaneously, i.e. first and second measurements, from a single sensor element of the optical fiber or from a group of sensor elements from a population or bundle of optical fibers (see column 9, lines 23-57). The detector system may be equipped with a computerized data acquisition system and analytical program to enable a variety of different measurements to be made and diverse parameters to be measured (see column 13, lines 33-56). By examining the uniquely addressed transmission ends of fibers or groups of fibers, the addressed transmission ends can transmit unique patterns for rapid identification and measurement of target analytes by the sensor (see column 4, lines 21-25).

Pinkel et al. differ from the instant invention in failing to teach specific statistical analysis of measurements by determining and excluding outlying beads from subpopulations, calculating a mean and standard deviation between measurements, evaluating statistical validity on the measurements, evaluating the measurements using confidence intervals, performing hypothesis testing, performing cluster analysis of measurements, and performing comparative evaluation between statistical analyses, as recited in claims 31-39.

Bierre et al. disclose a method of multiparameter data analysis which employs analyzing data by construction of a population hierarchy, wherein cell populations are not mutually exclusive. Bierre et al. specifically obtained measurements to collect a

plurality of parameters for each particle (bead) in a sample and performed statistical analysis on the obtained measurements. Statistical analyses performed include calculating a mean and standard deviation for the measurements, evaluating statistical validity of the measurements by defining and selecting particles into mutually exclusive clusters and subclusters, i.e. cluster analysis, and repeating statistical analysis for purposes of comparing and evaluating confidence intervals between measurements. See claims 1-3, 6, 11, and 12.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Bierre into the method of Pinkel using optical fiber array having a plurality of subpopulations to simultaneously measure the presence of target analytes in a sample because Bierre specifically taught that statistical analysis of cell or particle populations such as those in an array as in the method of Pinkel, presents a user with great flexibility in defining distinct and overlapping populations of particles or beads for use in subsequent examination. Additionally, statistical analysis, i.e. calculating mean/average, standard deviation, precision/ repeatability of a method as reflected in a second analysis, confidence intervals, correlation studies, and distribution/cluster analysis is part of standard laboratory practice and required in optimization procedures; hence, it would have been obvious for one of ordinary skill to use statistical analysis strategies known and conventionally used in chemical and immunological art to evaluate measurements obtained from a known method.

8. Claims 20-22 and 47 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al. (US Patent 5,837,196) in view of in view of Bierre et al. (US Patent 5,739,000), as applied to claims 27, 29-39 and 47 above, and in further view of Stimpson et al. (US Patent 5,559,668).

Pinkel et al. and Bierre et al. have been discussed supra. Pinkel et al. and Bierre et al. differ from the instant invention in failing to teach that the sensor elements are beads in an array dispersed on a substrate selected from glass or plastic.

Stimpson et al. disclose a waveguide binding assay method wherein an array comprising a plurality of subpopulations of light scattering beads (particles) are sensor elements for binding with target analytes (see Abstract and column 16, lines 27-64). The beads are colloidal metals such as gold and are dispersed on a substrate (waveguide or element) composed of either plastic or glass (see column 10, lines 33-59). Stimpson et al. also disclose that location of each of sensor element within the arrays can be configured, located, and identified (see columns 11 and 12).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the light scattering beads for use as sensor elements as taught by Stimpson into the optical fiber array used in the method of Pinkel as modified by Bierre because Stimpson specifically taught that light scattering beads, used as sensor elements, can increase acquisition of data or results by two orders of magnitudes by simultaneous interrogation; thus, allowing simultaneous measurements of the beads at multiple sites of an array and permitting extremely rapid acquisition of data.

Response to Arguments

9. Applicant's arguments filed December 20, 2005 have been fully considered but they are not persuasive.

A) Applicant argues that neither Pinkel nor Bierre, alone or in combination even with Stimpson, teach or suggest the invention of claim 27 because Pinkel fails to teach or suggest obtaining individual response signals at each of the sensor elements from at least one of the first and second subpopulations, wherein the first subpopulation comprises sensor elements having the same first bioactive agent and the second subpopulation comprises sensor elements having the same second bioactive agent. Applicant specifically contends that the detector of Pinkel is only arranged to read the signal from single optical fibers or groups of optical fibers where all the optical fibers in a group bear the same species of biological binding partner. Applicant argues, therefore, that Pinkel's description of detecting signals from the sensor elements of a population having the same bioactive agent is limited to obtaining a single signal from the population as a whole and not to obtaining individual response signals at each of the sensor elements that have the same bioactive agent.

In response, in Pinkel's teaching that the detector [of Pinkel] is arranged to read a response signal from single optical fibers or from groups of optical fibers where all the optical fibers in a group bear the same species, it appears that Pinkel reads on the claimed invention, as amended, because in claim 27 step b), a response signal at the sensor elements of the optical fiber in the fiber optic bundle is produced, and in step c),

individual response signals from the sensor elements of the optical fiber in the fiber optic bundle are obtained, albeit simultaneously. If Applicant intends that the individual response signals are individually and separately obtained or measured for statistical analysis between each individual response signal from the sensor elements in the optical fiber, such should be clearly and specifically recited. As recited, claim 27 appears to read on the teaching of Pinkel, and in combination with Bierre and the combined teaching renders obvious the claimed invention.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
June 24, 2006